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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,603	07/01/2003	Colombe Chappey	11068-065-999	4793

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,603	CHAPPEY ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12,13,18-21,23-29,31 and 36-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12,13,18-21,23-29,31 and 36-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 14 December 2007 has been entered.

Claims 2-11, 14-17, 22, 30 and 32-35 have been cancelled. Claims 1, 12, 13, 18-21, 23-29, 31 and 36-42 are pending and currently examined.

Objections

The objection to the specification under 35 U.S.C. §132(a) for introducing new matter into the disclosure is **withdrawn** upon further consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The New Matter rejection of claims 32 and 33 under 35 U.S.C. §112, first paragraph is **withdrawn** in response to the Applicants' cancellation of the claims.

The New Matter rejection of claim 1 under 35 U.S.C. §112, first paragraph is **withdrawn** upon further consideration.

New Rejection: Claims 1, 12, 13, 18-21, 23-29, 31 and 36-42 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites mutations at various position numbers as conferring "reduced susceptibility" to amprenavir without reciting the reference HIV isolate or strain. Due to the error-prone replication of HIV, there are many quasi species with different nucleotide and amino acid sequences. Especially when insertion or deletion mutations occur during viral replication, the sequences of the quasi species differ substantially from one another that a skilled artisan would not know whether one position number in one strain is referring to the same position in another strain. Therefore, position numbers in the absence of a reference strain number is vague and indefinite. Furthermore, simply referring to a mutation at a position without a reference sequence is vague and indefinite. One skilled in the art would not know what is the wild type amino acid residue at each position because of the existence of so many HIV-1 subtypes and strains. Lastly, the word "reduced" is a relative term, which is meaningless without a standard to compare to.

Claims 12, 13, 18-21, 23-29, 31 and 36-42 are rejected because they depend from an indefinite claim 1.

An amendment adding a limitation similar to the phrase, "wherein the level of susceptibility, mutations and position numbers are compared to the protease sequence of the NL4-3 reference strain," would obviate the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1, 12, 15, 26, 27, 29, 34, 36, 37, 39, 40 and 42 under 35 U.S.C. §102(b) as being anticipated by Robinson *et al*. (2000) is **withdrawn** in response to Applicant's amendment.

The rejection of claims 1, 12, 29, 36 and 42 under 35 U.S.C. §102(b) as being anticipated by Condra *et al*. (1996) is **maintained and extended to claims 13, 18-21, 23-28, 31 and 37-41**.

The instant invention is a method for determining whether a human immunodeficiency virus type 1 (HIV-1) has an increased likelihood of having a reduced susceptibility to treatment with amprenavir (APV), comprising detecting whether the protease encoded by said HIV-1 exhibits the presence or absence of a mutation associated with reduced susceptibility to treatment with said protease inhibitor at amino

acid position 11, 32, 34, 43, 46, 47, 48, 50, 54, 71, 76, 82, 83, 84, 91 or 95 of an amino acid sequence of said protease, wherein the mutation at amino acid position 34 is Q, the mutation at amino acid position 43 is T, and wherein the presence of said mutation indicates that the HIV-1 has an increased likelihood of having reduced susceptibility to treatment with amprenavir, with the proviso that said mutation is not V32I, M46I, M46L, I47V, I50V, I54L, I54M, I54V, I54T, V82A, V82F or I84V.

Applicants argue that Condra *et al*. do not teach every element of the claims. Examiner does not concur. Condra *et al*. clearly teach cross-resistant mutations including A71V (Table 1, page 8272), which is used to assess the susceptibility of an HIV isolate to a protease inhibitor. Furthermore, the wherein clause reciting "the mutation at amino acid position 71 is L" is not given patentable weight because it does not materially affect the physical method step of detecting amino acid sequence mutation in the claimed invention. Therefore, Condra *et al*. anticipate the instant invention.

The rejection of claims 1, 12 and 42 under 35 U.S.C. §102(b) as being anticipated by Palmer *et al*. (1999) is **maintained and extended to claims 13, 18-21, 23-29, 31 and 36-41**.

The instant invention is set forth above.

Applicants argue that Palmer *et al*. do not teach every element of the claims, such as the K43T mutation, instead, Palmer *et al*. teach the K43N mutation. However, the wherein clause reciting "the mutation at amino acid position 43 is T" is not given

patentable weight because it does not materially affect the physical method step of detecting amino acid sequence mutation in the claimed invention. Palmer *et al.* anticipate the instant invention so long as it teaches a method for determining the sequence of an HIV-1 strain and the resistant mutations such as G48V, A71V and K43N (Table 1).

Applicant's arguments, see page 8, filed on 14 December 2007, with respect to the rejection of claims 17, 26-28 and 32-36 under 35 U.S.C. §102(b) as being anticipated by Colonno *et al*. (2000) have been fully considered and are persuasive. The rejection of claims 17, 26-28 and 32-36 is **withdrawn**.

The rejection of claims 14, 17, 30 and 36 under 35 U.S.C. §102(a) as being anticipated by Kempf *et al*. (August 2001) is **withdrawn** in response to Applicant's amendment.

Applicant's arguments, see page 9, filed on 14 December 2007, with respect to the rejection of claims 1, 12, 20 and 42 under 35 U.S.C. §102(a) as being anticipated by Kempf *et al*. (August 2001) have been fully considered and are persuasive. The rejection of claims 1, 12, 20 and 42 is **withdrawn**.

The rejection of claims 1, 12, 18, 19, 25, 29, 36, 37, 39, 40 and 42 under 35 U.S.C. §102(a) as being anticipated by Beerenwinkel *et al*. (June 2002) is **maintained and extended** to claims 13, 20, 21, 23, 24, 26-28, 31, 38 and 41. Applicants argue that

Beerenwinkel *et al*. do not teach every element of the claims. Examiner does not concur. Beerenwinkel *et al*. teach the HIV genotype and susceptibility to amprenavir by looking at 277 genotype-phenotype pairs. The wherein clauses in the instant claims are not given patentable weight because they do not materially affect the physical method step of detecting amino acid sequence mutation in the claimed invention. Therefore, Beerenwinkel *et al*. meets the claimed limitations.

The rejection of claims 1, 12, 26, 27, 29, 36, 37, 39, 40 and 42 under 35 U.S.C. §102(b) as being anticipated by Paulsen *et al*. (11 June 2001) is **maintained and extended to claims 13, 18-21, 23-25, 28, 31, 38 and 41**. Applicants argue that Paulsen *et al*. do not teach every element of the claims. Examiner does not concur. Paulsen *et al*. clearly teach amprenavir resistance-associated mutations such as V32I and V82I, which meet the limitations of "detecting whether the protease encoded by an HIV- 1 exhibits the presence or absence of a mutation associated with reduced susceptibility to treatment with amprenavir" in the instant claims. Therefore, the instant invention is anticipated by Paulsen *et al*.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 12, 13, 18-21, 23-29, 31 and 36-42 are rejected under 35 U.S.C. §103(a) as being unpatentable over Kempf *et al*. (August 2001).

The instant invention is a method for determining whether a human immunodeficiency virus type 1 (HIV-1) has an increased likelihood of having a reduced susceptibility to treatment with amprenavir (APV), comprising detecting whether the protease encoded by said HIV-1 exhibits the presence or absence of a mutation associated with reduced susceptibility to treatment with said protease inhibitor at amino acid position 11, 32, 34, 43, 46, 47, 48, 50, 54, 71, 76, 82, 83, 84, 91 or 95 of an amino acid sequence of said protease, wherein the mutation at amino acid position 34 is Q, the mutation at amino acid position 43 is T, and wherein the presence of said mutation indicates that the HIV-1 has an increased likelihood of having reduced susceptibility to treatment with amprenavir, with the proviso that said mutation is not V32I, M46I, M46L, I47V, I50V, I54L, I54M, I54V, I54T, V82A, V82F or I84V.

Kempf *et al*. teach lopinavir-resistant mutations, L71I/L/V/T (Table 3 and Table 4) and K43T (page 7467, right column, 2nd last line) as compared to the NL4-3 wild type isolate (page 7463, 2nd column, second last line). Kempf *et al*. further teach that the potential for cross-resistance of isolates selected by lopinavir-RTV to other protease inhibitors will require careful assessment. See the last paragraph on page 7468, 2nd column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the method of Kempf *et al*. toward the prediction of amprenavir susceptibility so that the amino acids at the same positions are identified

and compared to the NL4-3 reference strain to determine whether there is a mutation in a HIV-1. The skilled artisan would have been motivated to do so to be able to predict the susceptibility of the HIV-1 to the whole panel of protease inhibitors. There would have been a reasonable expectation of success, given the high potential for cross-resistance of isolates selected by one protease inhibitor to other protease inhibitors even when the phenotypic correlations seem low, as taught by Kempf *et al*. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Comment [BC1]: Why are there claims with no art rejection? As I explained before, the wherein clause does not carry any weight. Claim 1 says "detect...the presence or absence of a mutation" - it doesn't matter whether the mutation was found in the reference or not! The Condra reference, for example sequenced the full length of both strands of the protease gene and should be a 102 on all the claims.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/L. H./
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648